UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MARYLAND

HOSPIRA, INC.,

Plaintiff,

and

SANDOZ, INC.

Intervenor-Plaintiff

v.

SYLVIA MATHEWS BURWELL,
Secretary of Health and Human Services

MARGARET A. HAMBURG, M.D.,
Commissioner of Food and Drugs,

and

UNITED STATES FOOD AND DRUG ADMINISTRATION,

Defendants,

MYLAN INSTITUTIONAL LLC

and

PAR STERILE PRODUCTS, LLC

Intervenor-Defendants.

Civil Action No. 8:14-cv-02662-GJH

MYLAN INSTITUTIONAL LLC'S REPLY IN SUPPORT OF MOTION FOR RECONSIDERATION OF THE TEMPORARY RESTRAINING ORDER (ECF NO. 20) ENTERED AUGUST 19, 2014

INTRODUCTION

The opposition filings by Hospira and Sandoz are long on rhetoric, but light on reasoning. As Mylan explains below, their arguments regarding likelihood of success on the merits turn on a "foreseeable use" test that runs contrary to binding Fourth Circuit authority. Just as importantly, Hospira and Sandoz rely on a fundamental misreading of FDA's decision letter. Let there be no mistake: FDA made a scientific determination that there is no overlap "at all" between Mylan's ANDA label, which references only Procedural Sedation, and Hospira's ICU Sedation use code. Hospira itself, in a separate patent litigation, conceded repeatedly that its '867 patent *does not* cover the only use recited in Mylan's label, Procedural Sedation. As to harm, Hospira stands silent in response to Mylan's debunking of the exaggerated and misleading assertion that Hospira would suffer irreparable harm, and Sandoz's only claim to harm rests on a phantom loss of statutory exclusivity that will not in fact take place. As such, Hospira and Sandoz are not entitled to any injunctive relief at all, much less an emergency temporary restraining order. Finally, if the Court does issue some type of temporary restraining order, Hospira and Sandoz have not justified the extreme, unprecedented, and unnecessary remedies of recall and rescission.

ARGUMENT

I. Hospira and Sandoz Fail to Show Likelihood of Success on the Merits

When submitting an ANDA to FDA, a generic manufacturer includes a label for its proposed generic product that is the "same" as the brand label except for authorized changes, such as the omission of "an indication or other aspect of labeling protected by [a] patent." 21 C.F.R. § 314.94(a)(8)(iv). When the ANDA includes a section viii statement and carves out one or more approved indications, the generic applicant removes language from the label that is included in the brand company's label. Mylan did precisely that in this case. Here is how the "Indications for Use" on the Precedex® label and the Mylan label differ:

Precedex® Label

---------- INDICATIONS AND USAGE ----------

Precedex is a relatively selective alpha$_2$-adrenergic agonist indicated for:

- Sedation of initially intubated and mechanically ventilated patients during treatment in an intensive care setting. Administer Precedex by continuous infusion not to exceed 24 hours. (1.1)
- Sedation of non-intubated patients prior to and/or during surgical and other procedures. (1.2)

Mylan Label

---------- INDICATIONS AND USAGE ----------

Dexmedetomidine hydrochloride injection is a relatively selective alpha$_2$-adrenergic agonist indicated for:

- Sedation of non-intubated patients prior to and/or during surgical and other procedures. (1.1)

As permitted by law, Mylan deleted the ICU Sedation indication from the Precedex® label entirely. Mylan also deleted every reference to ICU Sedation throughout the label's other sections (*e.g.*, dosing and administration instructions, adverse reaction information). Hospira's original Use Code for the '867 patent was "Intensive Care Unit Sedation," and Hospira admits that its "old and new use codes have exactly the same scope." ECF No. 2-4, Ex. E at 15 (ECF No. 2-4 at 47); *id*. at 4 (ECF No. 2-4 at 36) (new use code "clarifying," but not "expanding," the original use code). Thus, there can be no argument that Mylan's label "overlaps" with Hospira's "Intensive Care Unit Sedation" use code.

Rather than confronting Mylan's label, Hospira improperly seeks to change the focus to whether some physicians *may* theoretically use Mylan's product in the ICU for Mylan's lone Procedural Sedation Indication. As explained below, the Fourth Circuit has expressly rejected this "foreseeable use" test urged by Hospira, and FDA has consistently done the same. The Supreme Court's decision in *Caraco*—which involved only a single approved use, not two

approved uses as in this case—is not to the contrary. For at least these reasons, Hospira thus has no likelihood of success on the merits.

A. Hospira mistakenly focuses on how Mylan's product might be used rather than on Mylan's ANDA labeling

Hospira urges that the relevant inquiry is whether it may be possible that someone *might* use Mylan's product in a manner that Hospira alleges is covered by the '867 patent use code, citing a declaration discussing procedures conducted in the ICU. ECF No. 65 ("Hospira Opp'n") at 17-18. This is wrong. The proper inquiry, as conducted by FDA, is whether *Mylan's label* overlaps with the '867 patent's use code, *not* whether someone downstream from Mylan might use its ANDA product in a way that Hospira—wrongly—claims overlaps with the use code. Should this Court entertain Hospira's notion that ICU Sedation is sedation that may be used by doctors in the ICU, this argument was soundly rejected by the Fourth Circuit in *Sigma-Tau Pharmaceuticals, Inc. v. Schwetz*, 288 F.3d 141 (4th Cir. 2002), which arose in the analogous context of approving generic drugs under the Orphan Drug Act "for an indication that was no longer protected by market exclusivity." *Id.* at 143. The drug—Carnitor—was approved by FDA for two uses, only one of which remained protected. *Id.* The Fourth Circuit held that FDA was correct in determining the intended use of a generic version of the drug "by relying primarily upon the proposed labeling provided by the [generic] companies." *Id.* at 146. Indeed, the Fourth Circuit observed that "no court has ever found that a product is 'intended for use' or 'intended to affect' within the meaning of the [FDCA] *absent* manufacturer claims as to that product's use." *Id.* at 147 (internal quotations omitted, emphasis added).[1]

[1] *See also Bristol-Myers Squibb Co. v. Shalala*, 91 F.3d 1493 (D.C.C. 1996) (holding that a generic manufacturer may omit labeling protected by the three-year exclusivity because the exclusivity would otherwise prevent the approved ANDA product from entering the market at all and expand the scope of exclusivity beyond that permitted by Congress).

In rejecting the "foreseeable use" test that movants now advance, the Fourth Circuit noted that "not only might [such a test] result in extensions of exclusivity periods that Congress never intended, but it also might frustrate the longstanding practice of Congress, the FDA, and the courts not to interfere with physicians' judgments and their prescription of drugs for off-label uses." *Id.* Moreover, the Fourth Circuit recognized that a "foreseeable use" test would "bar the approval of generic drugs, even for unprotected indications" and would add a "huge evidentiary hurdle to the generic drug approval process [that] would be profoundly anti-competitive." *Id.*; *see also Decl. of Brandon M. White in Supp. of Mylan's Reply Br.* ("White Decl."), Ex. 2 (FDA's response letter to Watson Laboratories, Inc.'s citizen petition, FDA Docket No. 2008-P-0069 (Jul. 28, 2008) at 11 (noting that the foreseeable use test rejected in *Sigma-Tau* "might extend exclusivity beyond what Congress intended")). The Fourth Circuit concluded by explaining that "[g]iven that the generics in this case are not allowed to have the same labeling as Carnitor while Carnitor is enjoying a second seven-year period of exclusivity for the treatment of [the remaining protected indication], Sigma-Tau's argument constitutes nothing more than another attempt to obtain market exclusivity for any and all uses of its drug, thereby preventing generic competitors from entering the market for any indication." *Id.* at 148 n.3.

Here, Mylan complied with FDA regulations, "omi[tted] an indication or other aspect of labeling protected by [a] patent," 21 C.F.R. § 314.94(a)(8)(iv), in this case ICU Sedation, and included Procedural Sedation as the *only* indication for which it sought approval. Hospira itself conceded before FDA that its amended use code did not "broaden the claimed method of use beyond 'intensive care unit sedation.'" ECF No. 2-3 at 10. FDA assessed Mylan's carve out, and in the exercise of its scientific judgment, determined that there is no ICU Sedation on Mylan's label, irrespective of how some physician might use Mylan's product. ECF No. 2-3 at

10-12; *see also Warner-Lambert Co. v. Apotex Corp.*, 316 F.3d 1348, 1356 (Fed. Cir. 2003) ("While a physician may prescribe an approved drug for any use consistent with acceptable medical practice, an NDA, and hence an ANDA, only approves a use for which safety and efficacy have been proven."). FDA's assessment that Mylan's labeling carved out a protected use (ECF No. 2-3 at 12) is consistent with FDA's past focus on the generic manufacturer's label in making this judgment, is derived from FDA's scientific expertise in assessing proposed uses, and is thus due substantial deference. *See Sigma-Tau*, 288 F.3d at 146 ("The broad deference due the agency is all the more warranted when, as here, the regulation concerns a complex and highly technical regulatory program, in which the identification and classification of relevant criteria necessarily require significant expertise and entail the exercise of judgment grounded in policy concerns.") (internal quotations omitted).

At bottom, there is no "overlap" between Mylan's approved use as described in its label and Hospira's Use Code. This is apparent from Hospira's own interactions with FDA. In its January 24, 2014 letter to FDA, Hospira informed FDA that "any pending section viii statement must be rejected under either the old or the new use codes, because they have exactly the same scope." ECF No. 2-4, Ex. E at 15 (ECF No. 2-4 at 47). But FDA found—and Hospira rightly states that "FDA, [is] the expert agency in these matters" (ECF No. 65 at 17)—that Hospira's use codes, new and old, are *limited* to ICU Sedation. ECF No. 2-3 at 10. And Mylan's approved label does not include ICU Sedation. White Decl. Ex. 1 (Mylan's Dexmedetomidine label). Hospira nonetheless claims overlap exists "to the extent" that the product is used by doctors for Procedural Sedation "in the ICU setting." ECF No. 2-4, Ex. E at 5 (ECF No. 2-4 at 37); ECF No. 2-1 at 9-10. Setting aside that ICU Sedation is much more specific than any sedation in the geographic location of the ICU, Hospira's argument boils down to what doctors may do with

Mylan's product, not the approved use on Mylan's label. *See* Hospira Opp'n at 17-18 (claiming an overlap because Mylan's product "may at times" be used in the ICU—not that Mylan's label says that it *will* be). And as described above, this foreseeable use argument was explicitly rejected by the Fourth Circuit in *Sigma Tau* and has consistently been rejected by FDA in a number of generic drug approvals and written responses to citizen petitions.[2] When a label is silent as to an indicated use, it has been FDA's long-standing policy that there is no "overlap" and approval is given to the section viii applicant. *See* ECF No. 2-3 at 10-13. Because there is *no* overlap between Mylan's Procedural Sedation approved use as described in its label and Hospira's ICU Sedation use code, Hospira's merits argument collapses, finding no support in FDA law or practice. Indeed, FDA would have had to ignore its prior practice and Fourth Circuit precedent were it to embrace the theory Hospira advances in this action.

[2] *See* ECF No. 2-3 at 10-14; White Decl. Ex. 2 (FDA's response letter to Valeant Pharmaceuticals International's citizen petition, FDA Docket No. 2003P-0321/CP1 (Apr. 6, 2004)); Ex. 3 (FDA's response letter to Watson Laboratories, Inc.'s citizen petition, FDA Docket No. 2008-P-0069 (Jul. 28, 2008)); Ex. 4 (FDA's response letter to MedImmune Oncology, Inc.'s citizen petition, FDA Docket No. 2006P-0410/CP1 (Mar. 13, 2006)); Ex. 5 (FDA's response letter to King Pharmaceuticals, Inc.'s citizen petition, FDA Docket No. 2008-P-0304 (June 18, 2008)); Ex. 6 (FDA's response letter to Novo Nordisk Inc. and Caraco Pharmaceuticals Laboratories, Ltd.'s citizen petitions, FDA Docket Nos. 2008-P-0343 and 2008-P-0411 (Dec. 4, 2008)); Ex. 7 (FDA's response letter to Sandoz's citizen petition letter, FDA Docket No. FDA-2010-P-0087 (Aug. 3, 2010)); Ex. 8 (FDA's response letter to Savient Pharmaceuticals, Inc.'s citizen petition letter, FDA Docket Nos. 2005P-0383/CP1 & SUP1 (Dec. 1, 2006)); Ex. 9 (FDA's response letter to UCB, Inc.'s citizen petition letter, FDA Docket No. 2010-P-0545 (Feb. 24, 2011)); Ex. 10 (FDA's response letter to AstraZeneca LP's citizen petition letter, FDA Docket No. 2006-P-0073 (Nov. 18, 2008)); Ex. 11 (FDA's response letter to Unimed Pharmaceuticals, Inc.'s citizen petition letter, FDA Docket No. 2007-P-0169 (Apr. 25, 2008)); Ex. 12 (FDA's letter to AstraZeneca (Mar. 27, 2012)).

B. Movants place undue and misplaced weight on *Caraco* and fail to identify the law or rule from which FDA allegedly deviated

Hospira continues to misconstrue and place inordinate, and inappropriate, weight on a single phrase—in *dicta*—from *Caraco Pharmaceutical Laboratories, Ltd v. Novo Nordisk A/S*, 132 S. Ct. 1670, 1677 (2012). Hospira says that this single phrase both captures the Court's interpretation of section viii and provides the Supreme Court's understanding of FDA's "position, policy, and practice in interpreting and applying the statute." Hospira Opp'n at 19. A brief examination of *Caraco*—which arose from brand manufacturers' abusive practice of listing inaccurate use codes with FDA to delay generic competition—demonstrates that it does not stand for the sweeping proposition that Hospira and Sandoz assert.[3] Moreover, for the reasons noted above, there is no overlap "at all" between Mylan's ANDA labeling and Hospira's use code for ICU Sedation.

First, the *Caraco* Court followed its statement that "FDA will not approve such an ANDA if the generic's proposed carve-out label overlaps *at all* with the brand's use code," 132 S. Ct. at 1677 (emphasis added), with a citation to specific pages of the Preamble to an FDA final rule regarding amendments to 21 C.F.R. Part 314, 68 Fed. Reg. 36682-83. Those pages refer generally to the types of information patent holders must submit to facilitate, among other things, the section viii process, but nowhere there (nor anywhere else within the lengthy Preamble) is there any use of the term "overlap." Rather, the passage that comes closest to addressing the issue is as follows:

> Therefore, when an ANDA applicant has sought to *duplicate* the labeling for which the innovator has submitted the patent, and not to specifically omit, or

[3] In *Caraco*, the Court described brand manufacturers' "submission of inaccurate patent information to the FDA," and how "an overbroad use code … throws a wrench into the FDA's ability to approve generic drugs." *Caraco*, 132 S. Ct. at 1678, 1684.

> 'carve out' labeling, we require the ANDA applicant to submit a certification to that patent. A section viii statement would not be appropriate because the ANDA applicant is seeking approval *for exactly the same labeling* as that in the NDA for which the patent was submitted.

68 Fed. Reg. at 36682 (emphasis added). Here, of course, Mylan did *not* seek to duplicate the Precedex® label because it asked for—and FDA granted—approval for Mylan to carve out every reference in the label to the ICU Sedation indication.

FDA made clear in its decision letter in this case that it has consistently followed the practice of allowing ANDA applicants to carve out protected uses. ECF No. 2-3 at 10-13 (discussing carve outs allowed for repaglinide, tramadol, and oxandrolone).[4] The Supreme Court recognized this practice, stating that "[o]nly if the use code provides sufficient space for the generic's proposed label will the FDA approve an ANDA with a section viii statement." *Caraco*, 132 S. Ct. at 1677. Indeed, the Court's "overlaps at all" language makes sense in context—in *Caraco* there was only a single approved use for the drug in question, unlike here where Precedex is approved for two indications.[5] Here, FDA concluded that there was sufficient space for Mylan's proposed label: Procedural Sedation is not covered by the '867 patent's use code pertaining to ICU Sedation. ECF No. 2-3 at 14. FDA's decision, therefore, does not run counter to the *dicta* from *Caraco* relied on by Hospira. So even if the Court's "overlaps at all"

[4] FDA also cited its response in a letter decision (not a rulemaking) on a citizen petition filed by an NDA holder who protested a carve out of a protected use because, despite the carve out of the Use Code, the generic drug "will nonetheless be used as such." *See* White Decl. Ex. 3 at 1. This decision letter contains a lengthy discussion of section viii statements and describes FDA practice that is consistent with the practice followed here. *Id.* at 5-7.

[5] As explained at length in FDA's August 18 letter, ECF No. 2-3 at 10-13, FDA required Novo Nordisk to streamline repaglinide's three approved indications into a single indication: "as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus." *Id.* at 10; *see also Caraco*, 132 S. Ct. at 1689-90 (Sotomayor, J., concurring). This change engendered the controversy that resulted in the *Caraco* litigation.

statement constituted a careful explanation of FDA policy (it does not), it would make no difference here because ICU Sedation and Procedural Sedation are two distinct indications that are mutually exclusive; Hospira's use code covers the former and Mylan has included only the latter in its labeling. ECF No. 2-3 at 12.

Second, because the Supreme Court was not enunciating any "rule" in regard to overlap, and because Hospira and Sandoz have failed to point to language from any actual regulation from which FDA deviated, their claim that FDA engaged in rulemaking when it issued its August 18 decision is meritless. FDA followed longstanding practice. It did not deviate from settled law or a prior agency interpretation. It fashioned its decision mindful of the full context of the *Caraco* decision (rather than isolated *dicta*) and cited numerous past instances in which it had followed a similar course. In no sense could the decision letter trigger the notice-and-comment requirements of a rulemaking.[6]

[6] Plaintiffs insinuate that it was improper for Mylan to seek reconsideration of the likelihood of success on the merits in its motion. Hospira Opp'n at 10; ECF No. 62 ("Sandoz Opp'n") at 3 (internal pagination). Yet, in a heads-I-win-tails-you-lose argument, Plaintiffs also simultaneously characterize FDA's failure to challenge the likelihood of success as an admission that FDA's decision was contrary to law. Hospira Opp'n at 2. Not so. Neither Mylan nor FDA has conceded that any portion of Plaintiffs' claims have merit. ECF No. 52 at 2 n.1 ("The federal defendants are limiting their arguments herein to paragraphs 3 and 4 of the TRO, but intend to oppose Plaintiff's motion for a preliminary injunction and respond to the merits of Plaintiff's arguments."). Regardless, setting aside the two-faced nature of Plaintiffs' positions, Mylan asserts that it is necessary to address the entire basis for the Court's restraining order to determine whether emergency temporary relief or a preliminary injunction of any type is warranted and, if warranted, whether it is "narrowly tailored" to the claimed injury. *Hoechst Diafoil Co. v. Nan Ya Plastics Corp.*, 174 F.3d 411, 423 (4th Cir. 1999) (holding that a remedy provided by injunctive relief must be narrowly tailored to "protect only against the particular, threatened injury").

II. Hospira and Sandoz Failed to Rebut Mylan's Demonstration that They Will Not Suffer Irreparable Harm

The Supreme Court in *Winter v. Natural Resources Defense Council, Inc.*, 129 S. Ct. 365 (2008), made clear that a party must satisfy all four requirements for injunctive relief, including a demonstration that "irreparable injury is *likely* in the absence of an injunction." *Id.* at 375. "Indeed, the court in *Winter* rejected a standard that allowed the movant to demonstrate only a 'possibility' of irreparable harm because that standard was 'inconsistent with our characterization of injunctive relief as an extraordinary remedy that may ... be awarded [only] upon a clear showing that the [movant] is entitled to such relief.'" *Hines v. Maryland*, No. PJM-10-1260, 2010 WL 4273916, at *2 (D. Md. Oct. 27, 2010) (quoting *Winter*, 129 S. Ct. at 375–76).

Despite this requirement, Hospira's opposition said nothing to rebut Mylan's proof that Hospira in fact faces no irreparable harm. In response to Mylan's showing that Precedex® accounts for only 17% of Hospira's total U.S. pharmaceutical sales, not 98.4% as suggested by its moving papers, Hospira said nothing. ECF No. 39-1 ("Mylan Mem.") at 32-33 (internal pagination). Likewise, Hospira had no response to Mylan pointing out that on a July 30, 2014 earnings call, Hospira stated that it had already calculated the financial impact of a generic entry under a "carve-out process" and at no time suggested that this purely financial loss would result in irreparable harm to its business. Mylan Mem. at 34. Hospira's utter failure to prove that irreparable harm would be likely absent an injunction dooms its motion. *Hughes Network Sys., Inc. v. InterDigital Comm. Corp.*, 17 F.3d 691, 694 (4th Cir. 1994) ("Where the harm suffered by the moving party may be compensated by an award of money damages at judgment, courts generally have refused to find that harm irreparable."); *Teva Pharm. USA, Inc. v. Sandoz, Inc.*,

134 S. Ct. 1621 (Roberts, Circuit Justice, Apr. 18, 2014) (denying request for stay as the availability of money damages precluded a finding of irreparable harm).

For its part, Sandoz says it will suffer irreparable harm due to the "loss of its 180-day statutory exclusivity" and cites a number of instances in which Mylan has said, quite correctly, that the *unlawful* loss of statutory exclusivity can constitute irreparable harm. ECF No. 62 ("Sandoz Opp'n") at 3-4 (internal pagination). But there is nothing unlawful here; Sandoz failed to inform the Court that the 180-day exclusivity provision applies *only* against other ANDA applicants who file a Paragraph IV certification, not against those who file section viii statements. *Purepac Pharm. Co. v. Thompson*, 354 F.3d 877, 879 (D.C. Cir. 2004) (noting that the "statute and the implementing regulation create this exclusivity period by prohibiting the FDA from approving any other ANDA *that contains a paragraph IV challenge to the same patent*" for 180 days) (emphasis added).[7]

[7] In this regard, the two Mylan filings relied on by Sandoz to support its alleged irreparable harm are inapposite. *See* Sandoz Opp'n at 4. In fact, neither addresses a threatened loss of exclusivity by a Paragraph IV filer faced with a competing section viii certification. *See generally* ECF No. 62-3 (Mem. of Law in Supp. of Pl.'s Mot. for Preliminary Injunction, *Mylan Pharms. Inc. v. U.S. FDA*, Case No. 1:14-CV-75 (N.D.W. Va. Apr. 28, 2014)) (addressing exclusivity rights in the context of Paragraph IV certifications and reissue patents) & 62-4 (Decl. of Dr. S.K. Govil, *Mylan Labs., Inc. et al. v. Thompson*, Case No. 1:04-CV-01049-RBW (June 25, 2004)) (addressing exclusivity rights in the context of Paragraph IV certifications and pediatric exclusivity). Moreover, the actual district court decisions on these filings (omitted from Sandoz's brief) do not support Sandoz's irreparable harm claims. Quite the contrary, in *Mylan Pharmaceuticals, Inc. v. United States Food and Drug Administration*, No. 1:14CV75, 2014 WL 2339569 (N.D.W. Va. May 29, 2014), the district court found that loss of exclusivity was a mere economic injury and not irreparable harm. *See id.* at *12 (citing *Mylan Pharms. Inc. v. Sebelius*, 856 F. Supp. 2d 196 (D.D.C. 2012)); *Sandoz, Inc. v. FDA*, 439 F. Supp. 2d 26, 32 (D.D.C. 2006); *Apotex, Inc. v. FDA*, 2006 WL 1030151, at *16-17 (D.D.C. 2006)); *see also generally Mylan Labs., Inc. v. Thompson*, 332 F. Supp. 2d 106 (D.D.C. 2004) (silent as to Mylan's claims of irreparable harm based on loss of exclusivity).

The section viii carve out process is as much a part of the Hatch-Waxman Act as the Paragraph IV certification process. Congress clearly provided both mechanisms as ways to make generic drugs available to patients, but the two pathways "have quite different consequences." *Id*. at 880. A successful first Paragraph IV filer, like Sandoz, will be able to market its generic version of Precedex® for *all* approved uses—including the lucrative ICU Sedation indication—and will enjoy 180 days of exclusivity against all other Paragraph IV filers. By contrast, by filing a section viii statement carving out the ICU sedation indication, Mylan can market its generic drug immediately on FDA approval of its ANDA (irrespective of any Paragraph IV exclusivity), but *only* for Precedex's® Procedural Sedation indication.

Sandoz accuses Mylan of "line jumping," Sandoz Opp'n at 1, but the D.C. Circuit in *Purepac* provided an apt response to such laments. In that case a Paragraph IV filer complained that it had "played by the rules" by "fil[ing] a paragraph IV certification … thereby inviting an infringement lawsuit," while its competitor unfairly chose to file a section viii statement and avoid litigation. *Purepac*, 354 F.3d at 888. But the Court of Appeals found that the competitor "acted quite properly" in following the section viii pathway, rather than opting for a Paragraph IV certification. *Id*. The "fact that [the Paragraph IV filer] chose a *different—and ultimately unsuccessful—legal strategy*" did not mean that the section viii filer "flouted the rules." *Id*. (emphasis added).

If anything, it was Sandoz, not Mylan, that engaged in a "high risk/high reward" strategy. Sandoz filed a Paragraph IV certification asserting the invalidity of Hospira's '867 patent, in the hopes of being able to market its generic product for the ICU Sedation indication. Hospira then sued Sandoz, and in the ensuing litigation Sandoz obtained a judgment of invalidity of the '867 patent from the United States District Court for the District of New Jersey. *See Hospira, Inc. v.*

Sandoz Inc., No. 09-4951 (MLC), 2012 WL 1587688, at *30 (D.N.J. May 4, 2012). Hospira appealed to the Federal Circuit, but before the appeal was resolved, Sandoz and Hospira made the strategic choice to settle the litigation *on the condition that the district court vacate its invalidity judgment*. *See Hospira, Inc. v. Sandoz Inc.*, No. 09-4951 (MLC), 2014 WL 794589 (D.N.J. Feb. 27, 2014). In this way, both Hospira and Sandoz sought to have their cake and eat it too: beginning in December 2014 they made a private agreement to share the monopoly profits on Precedex®, and at the same time revive the invalid '867 patent to block other generic competitors from entering the market until the patent's expiration in 2019. However, their business decision to settle the litigation in no way can be deemed to effect the separate and distinct *rights* of other applicants.

By this maneuver, Sandoz would enjoy *years* of generic exclusivity, rather than a mere 180 days. Sandoz and Hospira, however, failed to account for the possibility that other generic companies might choose the "quite proper[]" section viii pathway and carve out the ICU Sedation indication. *Purepac*, 354 F.3d at 888. That is no justification for Sandoz to use its exclusive right to ICU Sedation as a toehold to prevent the lawful, safe, and effective use of Mylan's ANDA product for the separate Procedural Sedation indication. Besides this alleged, though thoroughly illusory, loss of exclusivity, Sandoz does not explain how it will be irreparably harmed. As with Hospira, this failure of proof precludes injunctive relief. *Winter*, 129 S. Ct. at 375–76.

III. Hospira and Sandoz Failed to Show that Paragraphs 3 and 4 of the August 19 Order (ECF No. 20) Are Authorized or Necessary

As to Paragraph 3 of the Order, the recall requirement, Mylan noted that FDA lacks authority to issue recalls absent an issue with the safety, branding or efficacy of a drug product, citing among other things 21 C.F.R. §§ 7.40 & 7.45. Mylan Mem. at 27-28. In response,

Hospira and Sandoz cite a number of cases standing for the unremarkable proposition that FDA has authority to recall adulterated or misbranded drugs or drugs that were not produced using Current Good Manufacturing Practices. Hospira Opp'n at 12; Sandoz Opp'n at 14 (citing *United States v. Barr Labs., Inc.*, 812 F. Supp. 458 (D.N.J. 1993)).[8] Equally inapposite are the injunctions Hospira and Sandoz cite involving trade dress or patent infringement cases in which defendants have been found to liable. *See* Hospira Opp'n at 13; Sandoz Opp'n at 14 (citing *Ortho McNeil Pharm., Inc. v. Barr Labs., Inc.*, No. 03-46-78 (SRC), 2009 WL 2182665 (D.N.J. July 22, 2009)).[9] Notably, Mylan is not an adjudged infringer, and Hospira has not even asserted patent infringement against Mylan. Indeed, in the patent infringement action between Hospira

[8] *See* Hospira Opp'n at 3-4, 12 (citing *United States v. Bowen*, 172 F.3d 682, 689 (9th Cir. 1999) (upon motion by the government, ordering recall of "adulterated" medical devices, *i.e.*, devices sold without FDA approval); *United States v. Barr Labs., Inc.*, 812 F. Supp. 458, 489 (D.N.J. 1993) (upon motion by FDA, ordering recall of products to protect the public health and safety where products had batch failure rates of up to 44%); *United States v. K-N Enters., Inc.*, 461 F. Supp. 988, 990-91 (N.D. Ill. 1978) (recalling unapproved and improperly manufactured products upon motion by government); *United States v. Lit. Drugs Co.*, 333 F. Supp. 990, 997-1000 (D.N.J. 1971) (recalling product where government inspections revealed unsafe manufacturing, manufacturer conceded mistakes, defendants attempted to evade compliance, and history of repetitive violations endangered the public safety); *United States v. Lanpar Co.*, 293 F. Supp. 147, 155 (N.D. Tex. 1968) (ordering recall where products not produced using good manufacturing processes to ensure safety and quality upon motion by government)).

[9] *See* Hospira Opp'n at 13 (citing *Boehringer Ingelheim Vetmedica, Inc. v. Schering-Plough Corp.*, 106 F. Supp. 2d 696, 709 (D.N.J. 2000) (ordering recall of products still in defendants' possession, and those in possession of customers "to the extent" customers chose to return them, after defendant was found to infringe plaintiff's patent at trial); *Rohm & Haas Co. v. Cumberland Corp.*, 220 U.S.P.Q. 978 (S.D. Tex. 1983) (ordering recall where defendant consented to an injunction, court found there was "[n]o doubt" that defendant infringed the asserted patent, and infringer was unable to pay damages); *Rhone-Poulenc Rorer Pharms., Inc. v. Marion Merrell Dow, Inc.*, 93 F.3d 511 (8th Cir. 1996) (ordering a corrective message be sent to physicians etc. where party was found at trial to have engaged in false advertising); *Perfect Fit Indus., Inc. v. Acme Quilting Co.*, 646 F.2d 800, 805-06 (2d Cir. 1981) (ordering voluntary recall of product where found at trial to violate trade dress rights)); *see also* Sandoz Opp'n at 14 (citing *Ortho McNeil Pharm., Inc. v. Barr Labs., Inc.*, No. 03-46-78 (SRC), 2009 WL 2182665 (D.N.J. July 22, 2009) (ordering a recall of products where defendant was found to infringe patents at summary judgment)).

and Sandoz, Hospira repeatedly represented to both the district court and the Federal Circuit that "Precedex's second indication [i.e., Procedural Sedation] is not covered by the '867 patent." *See* ECF No. 39-2, Ex. 3 (Transcript from *Hospira, Inc. v. Sandoz Int'l*, No. 09-cv-4591, ECF No. 397 (D.N.J. Apr. 5, 2012)) at 147-48 (ECF No. 39-2 at 168-169); *Hospira, Inc. v. Sandoz Inc.*, No. 12-1426, 2013 WL 298230, at *76-77 (Fed. Cir. Jan. 11, 2013) (Br. for Pls.-Cross Appellants Hospira, Inc.).

Having had more than ample opportunity to find precedent for their proposed recall, Hospira and Sandoz have failed to provide a single instance in which a court has ordered a recall due to some alleged (and speculative) procedural defect in an approval process, especially when the defect was not asserted until after a party had acted in reasonable reliance on an agency approval. It therefore remains the case that the recall requirement is unsupported, unprecedented, and unnecessary.[10]

As to Paragraph 4, Sandoz tacitly concedes that there is no need to order that FDA's approval be rescinded *ab initio*, saying nothing in defense of this provision. Hospira persists,

[10] Recalling product goes beyond an injunction to maintain the status quo: it constitutes a mandatory injunction for which a more demanding showing is required. The Fourth Circuit defines preliminary, prohibitive injunctions as those "aim[ing] to maintain the status quo"—*i.e.*, "the last uncontested status between the parties which preceded the controversy." *Pashby v. Delia*, 709 F.3d 307, 320 (4th Cir. 2013) (citation and internal quotation omitted). "Mandatory preliminary injunctions, which require actions and do not preserve the status quo, normally should be granted only in those circumstances when the exigencies of the situation demand such relief." *Wetzel v. Edwards*, 635 F.2d 283, 286 (4th Cir. 1980) (citations omitted). Both types of injunctions are "extraordinary remedies involving the exercise of very far-reaching power," *Pashby*, 709 F.3d at 319 (citation omitted), but the Fourth Circuit heightens its "exacting standard of review [to be] even more searching" when the preliminary injunction is "mandatory rather than prohibitory in nature," *id.* at 319 (citing *Sun Microsystems, Inc. v. Microsoft Corp.*, 333 F.3d 517, 525 (4th Cir. 2003). Indeed, where "mandatory relief is sought, as distinguished from maintenance of the status quo, … the facts and law [must] clearly support the moving party," particularly where the "relief … operates as deciding the case in favor of the movant." *Tiffany v. Forbes Custom Boats, Inc.*, 959 F.2d 232, 1992 WL 67358, at *6 (4th Cir. 1992) (unpublished) (citations and quotation omitted).

however, relying on *American Bioscience, Inc. v. Thompson*, 269 F.3d 1077 (D.C. Cir. 2001) (Hospira Opp'n at 15). In that case, the D.C. Circuit ordered the vacatur of FDA approval of an ANDA only *after* a final adjudication of the merits of the matter based on a full administrative record and review twice by the D.C. Circuit, not in the rushed context of a temporary restraining order. And even there, the D.C. Circuit did not order a recall of the generic products that had been put on the market.

Moreover, Hospira has again failed to explain why rescission *ab initio* is necessary here, nor has it responded to the numerous problems that such a rescission would create that counsel for FDA described during the August 20, 2014, telephonic conference. As but one example, Hospira does not address the tremendous waste of time that rescission would create, thus guaranteeing that Hospira and Sandoz will be free from—and the public denied—Mylan's competing product for the foreseeable future. It thus remains the case that Paragraph 4 is not a narrowly tailored remedy, and the Court should not impose it in the form of injunctive relief.[11]

Finally, in relying on opinions ordering the recall of unsafe, unapproved, adulterated, or infringing products, Plaintiffs argue misleadingly that Mylan's actions are similarly illicit—that Mylan placed product "on the market illegally." Hospira Opp'n at 11; *see also* Sandoz Opp'n at 11 (stressing Mylan's purported continued "unlawful conduct").

This is nonsense—and only underscores the unwarranted reputational harm Mylan would suffer if a recall were ordered. With regard to the purported illegality of Mylan's conduct, there was nothing untoward about Mylan's market entry—indeed, Plaintiffs have not identified a single action taken by Mylan in violation of any law. Rather, after filing all proper regulatory

[11] Arguably, the Court's August 19 Order, ECF No. 20, was tantamount to a preliminary injunction since it would afford complete and absolute relief to plaintiffs, relief that could not be unwound if the Court ultimately decided in FDA's favor.

applications, and after thorough and painstaking review by FDA *over a period of years*, FDA approved Mylan's ANDA. This approval granted Mylan the legal right to sell its generic product. That the Court may later find that FDA's approval of Mylan's ANDA was contrary to law (it was not) does not *ex post facto* transform Mylan's prior, legal, FDA-approved sale of products into illegal conduct. Such a ruling by this Court—finding unlawful conduct that was at the time of occurrence fully authorized under statute—runs afoul of foundational principles of fairness. *Cf.* U.S. Const. art. I, § 9, cl. 3 ("No bill of attainder or ex post fact Law shall be passed."). This is particularly so given that neither Hospira nor Sandoz has even attempted to challenge directly FDA's approval of Mylan's ANDA product (which approval makes no mention of FDA's August 18 decision letter) as safe and effective. As such, the spurious insinuations of "illegal" activity are particularly disconcerting where, as here, Mylan was not given a meaningful chance to respond to Hospira's hastily filed (and hyperbolic) papers in support of its requested restraining order—papers filed against FDA with *no notice to Mylan.*

Regardless, as noted above, the recall cases relied on by plaintiffs are far afield and not relevant. Contrary to these cases, Mylan's product was shipped with full FDA approval. There is certainly no evidence that the product is in any manner adulterated or unsafe—quite the contrary, in approving Mylan's ANDA, FDA found Mylan's product safe and effective. And Mylan has not infringed any patent—indeed, there has been no accusation of patent infringement, let alone a trial on the merits. Thus, despite claims that the court's power to order FDA to recall Mylan's product is "clear" (Hospira Opp'n at 12), Plaintiffs fail to advance a single instance in which such a recall order has issued—a recall of FDA-approved, safe, and effective products manufactured and sold by a party acting well within the confines of the law.

CONCLUSION

In the end, absent any precedent, Plaintiffs ask this Court to take the extraordinary step of ordering FDA to rescind Mylan's approval and recall its product despite having failed to identify *any* wrongful action taken Mylan. This bears emphasis: Mylan has engaged in no wrongful or illegal conduct—vis-à-vis Hospira, Sandoz, or anyone else—by launching its FDA-approved product. Plaintiffs do not contend otherwise, but rather make the remarkable claim that before launching, Mylan should have been content to wait "to see if litigation would be filed" against FDA. Hospira Opp'n at 21. To the contrary, Mylan was entirely within its rights to launch its product. Accordingly, for the foregoing reasons, and those stated in its opening memorandum, Mylan requests that this Court reconsider and withdraw its temporary restraining order *in toto* pending expedited briefing on a preliminary injunction, or, at a minimum, strike from the current Order Paragraphs 3 and 4.

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Respectfully submitted,

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